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EFFECT OF INCREASING PARITY ON SOME OBSTETRIC CONDITIONS

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From the Department of Obstetrics, the Johns Hopkins University and Hospital

Received for publication December 1, 1932

In a recent communication the author has demonstrated that in a series of 15,370 consecutive deliveries at the Johns Hopkins Hospital, both foetal and maternal death-rates were higher in the multiparous than in the primiparous patients of the group. It was also found that, from an optimal low figure between the ages of 17 and 19 years, there was a progressive rise in both foetal and maternal mortality as the age of the patient increased. These facts were found to hold true for the white and also for the black patients, although all mortality rates were significantly higher in the latter race.

These figures were obtained solely from patients delivered in the hospital and it was felt that their exact validity was open to some question owing to the high incidence of abnormal and referred emergency cases, particularly among the multiparous patients. Accordingly, it seemed advisable to reinvestigate the group, omitting all referred emergency admissions and including a large number of essentially normal women delivered in their homes by the Obstetric Service. It was felt that such a group would present a fairly normal cross-section of the child-bearing population, and that the results obtained would not be open to the criticism previously suggested. It was decided not only to separate primiparae from multiparae, but to subdivide the latter according to the exact parity, grouping together all patients of para 10 or above. The original racial division of whites and blacks was continued.

The series of cases comprising this study includes, accordingly, all patients registered for prenatal care in the hospital dispensary and subsequently delivered of a viable child on the hospital or outside service from the date of inception of the department in 1896 to January 1, 1931. The purpose of the analysis is primarily to determine the effect

of increasing parity, not only on the maternal and foetal death-rate, but also on the incidence of certain obstetric conditions and abnormalities. Differences observed between the white and black race are also shown. The following subjects have been investigated: maternal and foetal mortality rate; the incidence of breech and transverse presentations; eclampsia, nephritis, and total toxemia; placenta praevia, premature separation of the normally implanted placenta, and postpartum hemorrhage; pyelitis; multiple pregnancy; puerperal infection; operative delivery; the weight of the baby; and the mean duration of labor. It is felt that such a study, by including most of the commoner complications of pregnancy, would indicate the main reasons for any observed differences in maternal and foetal mortality according to parity.

TABLE 1

Total patients in series according to source and color

	HOSPITAL CASES	O.O.S. CASES	TOTAL
White	8894	5062	13,956
Black	8205	7066	15,271
Total	17,099	12,128	29,227

From the time that the Obstetric Service was first incorporated at the Johns Hopkins Hospital to January 1, 1931, 29,227 women were delivered at term either in the hospital or in their homes. By "at term" we mean that the child had attained either a weight of 2500 grams or a length of 45 cm., arbitrary figures used for indexing purposes on the service. The source of these cases according to race and place of delivery is shown in table 1. It will be noted that 17,099 (58.5 per cent) women belonged to the hospital population, as contrasted with 12,128 (41.5 per cent) who were delivered at home, and also that there were slightly more black patients (52.25 per cent) than white (47.75 per cent).

Table 2 indicates the division of these cases according to parity. In both races the primiparae make up just over one-third of the total group. Of these patients about one-seventh of the whites and one-fourteenth of the blacks were unregistered emergency cases, with an extremely high incidence of the various obstetric abnormalities.

These have been omitted from the further studies made, and there remain 26,034 patients to be used in the analyses, a group which we feel gives a fairly normal and representative population.

It may be said in passing that the gross maternal mortality rate for the entire series of 29,227 cases was 0.39 per cent, and was higher among the multiparae than the primiparae, rates of 0.33 per cent and 0.42 per cent being obtained, respectively. Likewise, the foetal mortality rate for the entire series was 5.30 per cent, and when only patients delivered spontaneously were included, was 3.26 per cent. Both of these foetal rates were much higher in the black than in the white

TABLE 2

Total patients in series according to parity and color

PARA	WHITE	BLACK	TOTAL
1	5114	5370	10,484
2	2606	3243	5849
3	1612	1885	3497
4	1192	1271	2463
5	860	902	1762
6	691	703	1394
7	588	498	1086
8	409	387	796
9	288	276	564
10–	596	736	1332
Total.....	13,956	15,271	29,227

race, but for the entire series the maternal death-rate was slightly higher among the whites (0.394 and 0.386 per cent).

We now come to the analysis of the 26,034 registered patients in the series.

1. *Maternal death-rate.* Figure 1 illustrates the maternal deaths per 1000 term deliveries for the series according to parity. In these and the subsequent figures certain paras are combined whenever the number of cases at hand for each specific para is too small to allow significant analysis. The lowest observed death-rate for the combined races is in the primiparous group, which increases slightly in the groups 2, 3, 4 and 5, 6, 7; but rises significantly when the parity reaches 8 and above. Indeed, the mortality per 1000 deliveries is almost twice as

high in the latter group as in the primiparous group, being 4.21 and 2.32, respectively. The total mortality rate is .257 per cent, or one death for 389 deliveries. Deaths occurring among the primparae amount to 1 in 431 deliveries; while the figure of 1 in 369 obtains for the total multiparae. Also, the mortality rate is higher in the black than in the white women, being 1 in 337 and 1 in 476 deliveries, respectively. This increased death-rate in the black race is due almost entirely to infection.

From the above figures it would seem that the primiparous woman offers the best mortality risk, and that, although very little increase is

FIG. 1

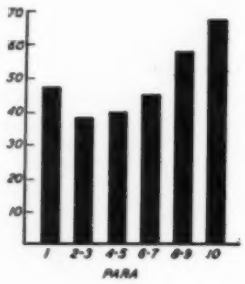

FIG. 2

FIG. 1. MATERNAL MORTALITY PER 1000 DELIVERIES ACCORDING TO PARITY
FIG. 2. FOETAL MORTALITY PER 1000 DELIVERIES ACCORDING TO PARITY

noted up to para 7, yet in women who have had 7 or more babies, the mortality rate is almost double that of the primiparous group.

2. *Foetal mortality rate.* The effect of increasing parity on the foetal mortality rate is shown in figure 2. The figures given here include both stillborn infants and neonatal deaths up to the fourteenth day of life. From a figure of 47.41 deaths per 1000 deliveries, the foetal deaths fall to an optimum of 38.36 for the para 2 and 3 group. From here, there is a steady rise, and when the parity reaches 8 and above, the rate is even higher than in the primiparous group. It will be noted that in the bracket para 10 and above, 67.69 foetal deaths occur per 1000 deliveries, 20 more than are to be observed in the primiparous group. The total foetal mortality for the series is 4.46 per cent, or approximately 1 in 22 deliveries. There is a slightly higher

rate among the total primiparae than among the multiparae, 1 in 21 and 1 in 23 deliveries, respectively. Also, the rate is significantly higher in the black (5.41 per cent) than in the white race (3.32 per cent).

In an effort to explain these differences according to parity, it was decided to analyze some of the commoner obstetric abnormalities in an effort to determine what part, if any, was played by them.

3. *Incidence of breech presentation.* Figure 3 illustrates the data accumulated on the incidence of breech presentation. It will be noted

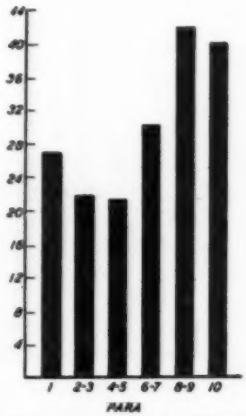

FIG. 3. INCIDENCE BREECH PRESENTATION PER 1000 DELIVERIES ACCORDING TO PARITY

that it occurs most frequently in the high para groups (6 and above). The total incidence for the series is 2.56 per cent, or 1 in 39 deliveries, figures rather lower than those usually observed. Very little difference in the incidence of total primiparae and multiparae is observed, though breech presentation seems to occur relatively more frequently in the former (2.66 per cent) than in the latter group (2.51 per cent). It is, however, interesting that the incidence is definitely higher among the white women (27.59 per 1000 deliveries) than among the black (23.97 per 1000). In view of the high incidence of contracted pelvis in the black race and since this condition is supposed to play an impor-

tant rôle in the etiology of breech presentation, such a finding is a surprising one.

It is our feeling that the increased incidence of breech presentation among the patients of para 6 and above may partially account for the increased foetal mortality found in such women.

4. *Incidence of transverse presentation.* The marked increase with parity in the incidence of transverse presentation, most particularly among those patients of para 10 and over, is shown in figure 4. Almost ten times as many transverses are seen in the latter group as in the

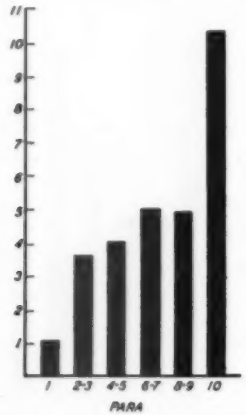

FIG. 4. INCIDENCE TRANSVERSE PRESENTATION PER 1000 DELIVERIES ACCORDING TO PARITY

primiparous portion of the series. This type of presentation occurs 3.3 times per 1000 deliveries, or in 1 case out of every 303. As was the case with breech presentation, the transverse is seen relatively oftener in the white than in the black race, the figures being 1 in 248 and 1 in 372 deliveries, respectively.

Thus, we find that transverse presentation may offer another explanation for the increase of foetal mortality with increasing parity. On the other hand, neither it nor breech presentation indicates any reason for the observed higher mortality in the colored race.

5. *Incidence of eclampsia.* As was to be expected, eclampsia was found to be mainly a complication of primiparity. Figure 5 shows

that increasing multiparity is not associated with a more frequent incidence of convulsive toxemia. This complication of pregnancy is seen five times more often in primiparae than in multiparae, the incidence per 1000 deliveries being 10.69 and 2.18, respectively. It occurs

FIG. 5. INCIDENCE ECLAMPSIA PER 1000 DELIVERIES ACCORDING TO PARITY

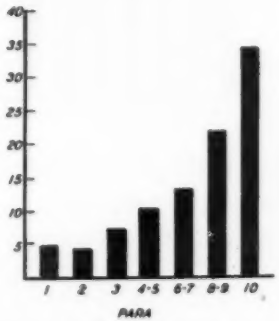

FIG. 6. INCIDENCE NEPHRITIS PER 1000 DELIVERIES ACCORDING TO PARITY

relatively more frequently among black women, being found once in 179 cases among them, and once in 216 cases among the whites.

6. *Incidence of nephritis complicating pregnancy.* Figure 6 illustrates clearly the marked rise in the incidence of nephritis with increasing

multiparity. Although this complication occurs only slightly more than twice as often among the total multiparae than among the primiparae (10.91 and 4.63 per 1000 deliveries), yet in the group of para 10 and above it is seen more than seven times as often (34.28 per 1000 deliveries) as in the primiparous portion of the series. Very little difference is observed in the incidence among the white and black races, although the condition apparently occurs somewhat more frequently in the whites.

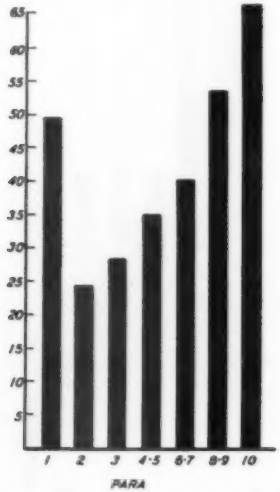

FIG. 7. INCIDENCE TOTAL TOXEMIA PER 1000 DELIVERIES ACCORDING TO PARITY

7. *Incidence of total toxemias.* The incidence of total toxemias is, of course, heavily weighted in the primiparous group by the cases of eclampsia, and among the higher multiparae by those of nephritis. However, figure 7 shows that, from an optimal low toxemia incidence in the para 2 group, there is a steady rise in frequency, and above para 7 the incidence is actually higher than is seen among women pregnant for the first time. Again, due to the cases of eclampsia, the incidence of total toxemia generally is higher in the primiparae than in the total multiparous group and is 49.50 and 34.37 per 1000 deliveries, respectively. Although the rate is slightly higher in the white than in the black race no significant difference is to be found between them.

It would seem, then, from an analysis of the toxemic conditions that they would influence to a considerable extent the observed differences in foetal mortality with increasing multiparity, and to a less marked degree the maternal mortality rates.

8. *Incidence of placenta praevia.* It is evident from a study of figure 8 that placenta praevia is not only a disease of multiparity but essentially one whose incidence increases in direct proportion to parity.

FIG. 8. INCIDENCE PLACENTA PRAEVIA PER 1000 DELIVERIES ACCORDING TO PARITY

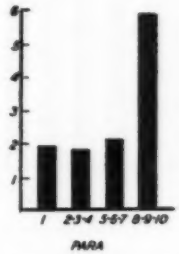

FIG. 9. INCIDENCE PREMATURE SEPARATION PER 1000 DELIVERIES ACCORDING TO PARITY

Thus, in the group of para 8 and above, it is seen more than four and one-half times as often as in primiparae. The incidence of placenta praevia for the entire series is 0.173 per cent, or 1 in every 578 cases. In primiparae it occurs only once in 1010 deliveries, as contrasted with a figure of 1 in 472 for total multiparae. This complication occurs more frequently in the white race (1 in 495) than in the black (1 in 676).

9. *Incidence of premature separation of the normally implanted placenta.* Premature separation also is encountered more frequently among multiparae, as is shown in figure 9. Here, however, we find no

significant increase in incidence until the group of para 8 and above is reached, when the rise becomes very sharp. It is interesting to note that in this series premature separation occurred somewhat more frequently than did placenta praevia and was noted once in every 448 deliveries. The ratio of total primparae to multiparae is 1.87 and 2.42 per 1000 cases, respectively. As with placenta praevia, it occurs less often in the black race (1 in 488) than in the white (1 in 410).

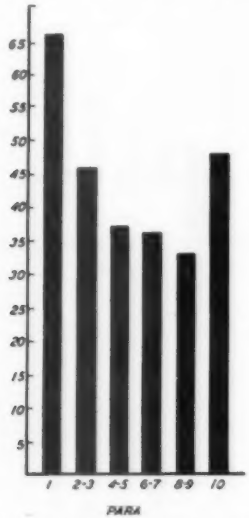

FIG. 10. INCIDENCE POSTPARTUM HEMORRHAGE PER 1000 DELIVERIES ACCORDING TO PARITY

10. *Incidence of postpartum hemorrhage.*[1] It was expected that postpartum hemorrhage would occur more frequently with increasing parity, since atony of the uterus might be thought to occur oftener in a woman who had had several pregnancies. That such is not the case, however, may be noted from figure 10. With the exception of the group para 10 and above in which an increase is noted, there is a continuous decrease as the higher paras are reached. Postpartum hemorrhage occurs in this series 66.04 times per 1000 deliveries in the

[1] In this series we have adopted the arbitrary standard of 600 cc. or more of blood as constituting a postpartum hemorrhage.

primiparous group as contrasted with 41.74 per 1000 among the multiparous group. It also is seen more frequently in the white race (57.36 per 1000) than in the black (44.19 per 1000).

Thus it seems evident that the three common obstetrical complications due to hemorrhage would affect the mortality rate for the mother

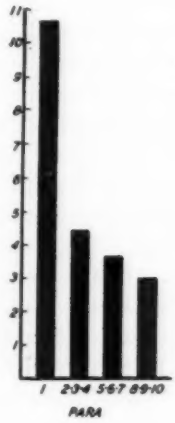

FIG. 11

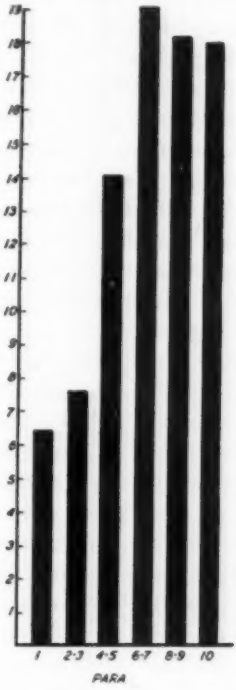

FIG. 12

FIG. 11. INCIDENCE PYELITIS PER 1000 DELIVERIES ACCORDING TO PARITY

FIG. 12. INCIDENCE MULTIPLE PREGNANCY PER 1000 DELIVERIES ACCORDING TO PARITY

and child more in the whites, although for both races placenta praevia and premature separation would seem to play a significant part in the higher rates seen with increasing multiparity.

11. *Incidence of pyelitis.* Figure 11 indicates that pyelitis occurs most often in primiparae, and with decreasing frequency as multi-

parity increases. The incidence of this complication for the entire series is 6.26 per 1000 deliveries, or once in 160 cases. It also is found more frequently in the white race (1 in 140) than in the black (1 in 181).

12. *Incidence of multiple pregnancy.* Because of the high foetal mortality associated with multiple pregnancy, the analysis shown in figure 12 was made. This indicates that twins or triplets occur about twice as often among multiparae, and that the incidence is highest among patients of para 6 and above. Multiple pregnancy occurred once in every 99 cases for the entire series and was seen slightly oftener in the white race (1 in 94) than in the black (1 in 105).

13. *Incidence of puerperal infection.* The diagnosis of puerperal infection is made in this Clinic whenever the sublingual temperature reaches 100.4°F. on two (not necessarily successive) days in the puerperium, excluding the first day after delivery and providing other causative factors such as respiratory infection, pyelitis, etc., cannot be elicited. In this series infection occurred in 10.71 per cent of all cases. This high rate would seem to be due to the fact that the vast majority of our material comes from the lowest stratum of society—tenement districts of a large city. Less than 5 per cent of the women were of the private patient type.

That the highest incidence of puerperal infection occurs among primiparae is illustrated in figure 13, and is found to be about three times as great among them as in the multiparous population, being 18.43 and 6.58 per cent for the two groups, respectively. This is undoubtedly accounted for to a great extent by the differences in operative incidence for the two classes. There appears to be a steady decrease in infection until an optimum in the group para 5 is reached, after which the incidence tends to increase slightly. Figure 13 also indicates the constantly higher morbidity rate among the colored population. That this is a true racial difference is indicated by the fact that the operative incidence is lower among the black than the white women. It has already been noted that the increase in maternal mortality in the colored race over that obtaining in the white is almost entirely explained on the basis of deaths from puerperal infection.

14. *Incidence of operative delivery.* Naturally the highest incidence of operative delivery is to be found among primiparae, as is shown in figure 14. An optimal low incidence is reached in the para 4 and 5

group, following which a steady and rather sharp increase occurs. This is probably due in great part to the increased frequency in the higher para groups of some of the abnormalities already noted, such as placenta praevia and premature separation. Since both foetal and

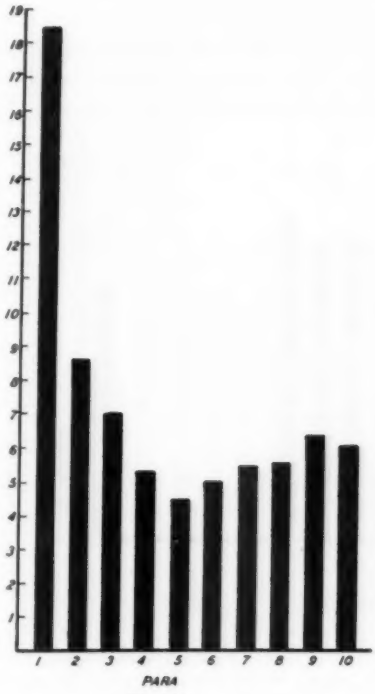

FIG. 13

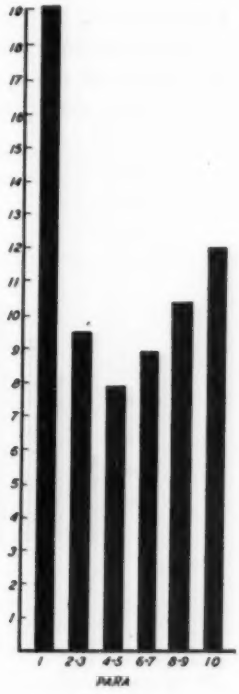

FIG. 14

FIG. 13. INCIDENCE PUERPERAL INFECTION PER 1000 DELIVERIES ACCORDING TO PARITY

FIG. 14. INCIDENCE OPERATIVE DELIVERY PER 1000 DELIVERIES ACCORDING TO PARITY

maternal mortality risks are increased with operative delivery, again we have an explanation for the higher rates noted in the higher para groups.

Although contracted pelvis occurs more than three times as often in

the colored as in the white patients on the service, yet the operative incidence is definitely higher in the latter group—10.81 and 14.94 per cent, respectively. This is undoubtedly to be explained by the smaller size of the infant and the increased malleability of the head of the black baby. The total operative incidence for the entire clinic is 12.78 per cent.

15. *Mean weight of baby.* Figure 15 indicates the effect of parity on the weight of the infant at birth. The average multiparous child weighs 202 grams or approximately $6\frac{2}{3}$ ounces more than that of the

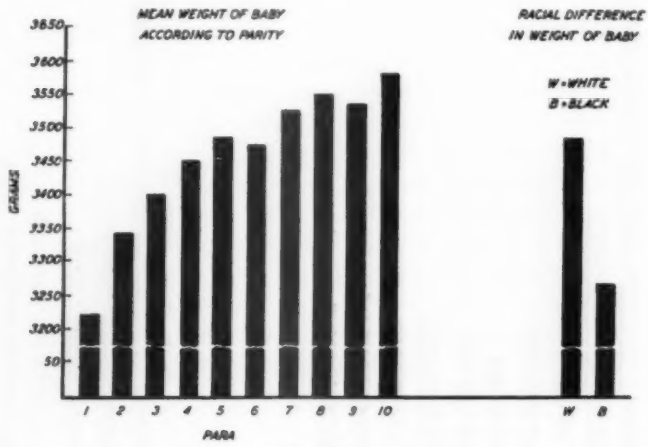

FIG. 15

primipara. Moreover, a fairly steady rise of weight is noted with increasing multiparity so that the mean weight in the group para 10 and over is 363 grams or 12 ounces more than that of the para 1 group. It is felt that these findings possess considerable significance. On the one hand, they afford additional explanation for the increased foetal mortality in the higher para groups and also serve as a warning against judging too lightly a case of moderate pelvic contraction merely because the patient has had one or more babies spontaneously.

Our figures also indicate the marked discrepancy between the mean weight of the black and white infants in the series, since the black baby

averages 169 grams less for primiparae and 249 grams less for multiparae than does the white. It is felt that the smaller size of the black infant is probably due to the fact that the colored population of the series is made up essentially from women of several generations of city

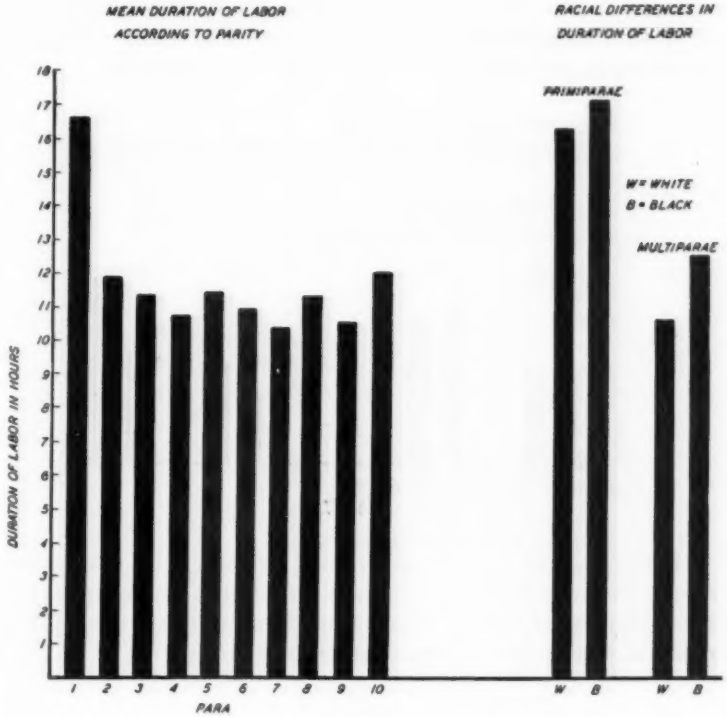

FIG. 16

dwelling under unsatisfactory hygienic conditions. An illustration of this is an incidence of almost 20 per cent of rachitic pelvis in this race. Thus, the smaller black baby is believed to be an evidence of physical degeneracy rather than one of inherent racial difference.

16. *Mean duration of labor.* It has been asserted that the mean

duration of labor rises sharply in the higher multiparous groups. That such is not the case in this series is shown by figure 16, since no significant changes in duration are to be found among the multiparae of either race. The total labor for the primiparae is 16.58 hours and for the multiparae 11.44 hours. For both primiparae and multiparae the labor lasted definitely longer in the black than in the white patients; still another explanation for the higher foetal mortality among the former patients.

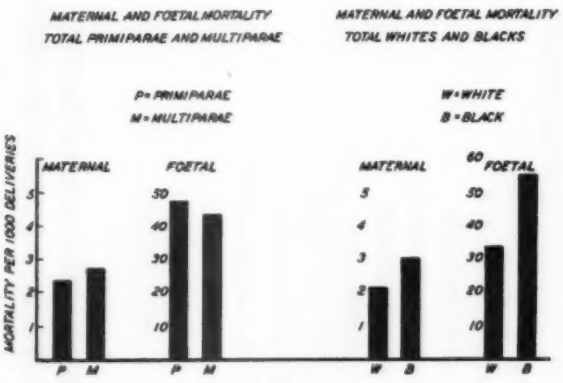

FIG. 17

17. *Gross racial and parous differences.* Figures 17, 18, and 19 indicate in composite form the differences according to race and parity for the various items studied. Since these differences have already been noted, no further comment on them seems necessary.

SUMMARY

In an analysis of a series of 29,227 consecutive deliveries at or near term on the Obstetrical Service of the Johns Hopkins Hospital, it was found that both maternal and foetal mortality rates rise with increasing parity of the patient. In the multiparous groups the maternal rate is constantly higher than in the primiparous groups. While following an optimum in the para 2 and 3 group the foetal rate constantly rises and with para 8 and above is higher than among the primiparous

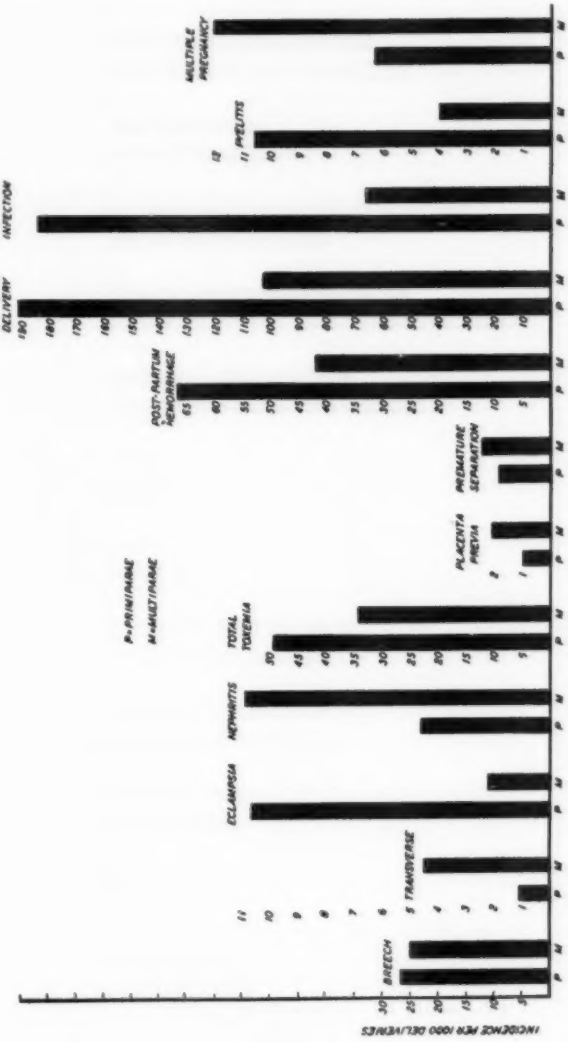

FIG. 18. INCIDENCE OF VARIOUS ITEMS STUDIED; TOTAL PRIMIPARAE AND MULTIPARAE

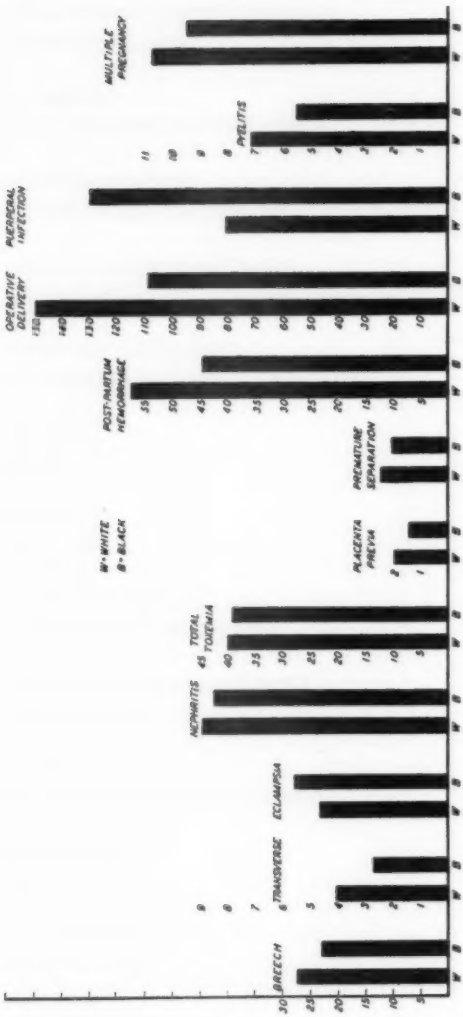

FIG. 19. INCIDENCE OF VARIOUS ITEMS STUDIED; TOTAL WHITES AND BLACKS

population. Also, both maternal and foetal mortality is significantly higher in the colored than in the white race.

Further analyses were made of some of the commoner obstetric complications in an effort to elicit some explanation for the above findings. The results are as follows:

1. There is a definite increase in the incidence of breech presentation in the para 6 group and in those above. This type of presentation is seen more frequently among the whites than the blacks.

2. Transverse presentation occurs rarely among primiparae and becomes increasingly common with rising multiparity. It also is seen more often in white patients.

3. Eclampsia is predominately a disease of primiparity and no increase is found with high multiparity. It occurs somewhat more frequently in the black race.

4. Nephritis increases in direct ratio with multiparity and undoubtedly plays a significant rôle in the death-rate for the high para groups. Very little racial difference is to be noted.

5. The incidence of total toxemias is high among primiparae. However, following an optimal low rate in the para 2 group, there is a rapid and steady increase; and for para 8 and above the figures are higher than those pertaining to the para 1 group. Again, very little racial difference is discernible.

6. Placenta praevia is mainly a complication of multiparity and the incidence increases with it. This condition is seen somewhat more frequently in the white race.

7. Premature separation of the placenta occurs in about the same ratio for the para 1 to 7 groups. Above this, it is definitely increased. It also is slightly more common in the white race.

8. The incidence of postpartum hemorrhage is higher among primiparous women. From this point a steady decrease is noted, except in the para 10 group and above, where there occurs a rather sharp rise. It is seen much more commonly in the white race.

9. Pyelitis is commonest among primiparae and decreases with increasing parity. It, too, is seen more often among white patients.

10. Multiple pregnancy is apparently most apt to occur in women of para 6 and above, and is least often met with in primiparae. It is seen slightly oftener in white women.

11. Puerperal infection occurs most frequently in primiparae. It decreases steadily until the para 5 group is reached and then rises somewhat. It is much more common among the blacks and is the chief explanation of the increased maternal mortality in that race.

12. The highest incidence of operative delivery is obviously to be found among the primiparae. However, following a decrease to an optimal low for the para 4 and 5 groups, there is a steady and rather rapid rise. Operative delivery occurs much more commonly in the white race.

13. The smallest infants are born to primiparae. There is a steady rise in weight with increasing multiparity so that the average child born to a woman of para 10 or more weighs 12 ounces more than that of the primipara. The children of white women average several ounces heavier than those of the black.

14. Although the mean duration of labor is naturally several hours more in primiparae than in multiparae, no significant change is to be noted with increasing multiparity. The average labor is definitely longer in the black than in the white woman.

(The statistical tables on which this article is based have been omitted owing to lack of space.)

SOME ASPECTS AND PROBLEMS OF INTRACRANIAL PRESSURES[1]

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It is perhaps fitting that an anatomist should respond to an invitation to deliver this lecture under surgical auspices, for in the career and interests of David Hayes Agnew there is much justification for an anatomical presentation. Dr. Agnew was a great and skillful surgeon whose early professional years were enthusiastically devoted to the dissecting room in the old Philadelphia School of Anatomy. There extramural teaching flourished under the leadership of Dr. Agnew who became a brilliant expositor of gross human anatomy, as well as a true student whose scientific curiosity ranged into the then relatively unexplored field of man's relation to the rest of the animal kingdom. Dr. Agnew's technical approach to the subject and his outstanding gift of demonstration made the School of Anatomy an unique and successful experiment in American medical education: his decade of activity there was characterized by increasing enrollments of students and by the best of morphological teaching of the day. With the diversions of undertakings due to the Civil War, Dr. Agnew came into this University as Demonstrator of Anatomy—a post for which he was particularly well suited. It was a great period in Philadelphia anatomy, revolving as it did about the admirable work and widespread personal influence of Joseph Leidy. It was a medical generation when surgery rested so fundamentally upon detailed information from gross anatomy, when pathology was just beginning to afford a useful basis for surgical procedure. To this era Dr. Agnew contributed largely: his interests and accomplishments were those of the period when anatomy was a far less wideflung subject than it is today. But in a morphological approach to the problems of his clinical subject, Dr. Agnew could not fail to have a profound understanding, today as well as yesterday.

[1] The D. Hayes Agnew Lecture, delivered at the School of Medicine, University of Pennsylvania, February 10, 1933.

Modern surgery—or better, present-day surgery—demands far more than merely a morphological background. It has passed through the era when pathology made its great and continuing contribution, and now it is demanding much of physiology, not only from the chemical and physical aspects but also from the so-called experimental angle. And here it is that surgery and anatomy again come into close relationship, with the development of anatomy into the various correlated fields of experimental morphology—into all of those subdivisions of medical science where knowledge of normal structure is necessary for an understanding of function. The critically minded observer may indict this conception of the scope and extent of anatomy; but I would reply, as did Woollard (21) some years ago, defining "the content of any particular science as what those who enjoy the title of that particular science are interested in." It is because of my belief in this general thesis that I as an anatomist have accepted the great honor of giving the Agnew Lecture this year, in the hope that there is in today's anatomy something which has definite relationship to surgical problems—something which may underlie in a basic way certain of the current questions of surgical procedure.

One of the great subdivisions of modern surgery is of course that of the nervous system. It is here also that experimental anatomy has been delving for the last few decades; it is here that fundamental physiological and anatomical concepts have so much to do with one of the chief problems of surgical procedure and surgical management. Neurological surgery has always to give final consideration not to technique but to the control of intracranial pressure. Nothing can be undertaken within the bony encasement of brain and spinal cord which does not find relation to the fluid-systems of the central nervous system. And while for many years we have been content with knowledge of these pressure-relationships within the cranium as derived from experiments based upon four-footed mammals whose customary posture is horizontal, we are awakening to the fact that man, and perhaps certain others of the primate order, have their own peculiar group of problems of pressure about the central nervous system, due primarily to the fact that man maintains the erect posture for two-thirds of his time. Today we are just beginning to take cognizance of the fact that this change from a horizontal to an erect position has given rise to

questions which, while not solely those of the erect animal, still affect profoundly all of our current ideas of intracranial tension.

In the primitive vertebrates no part of the central nervous system is habitually carried at levels above those of the rest of the system and a strictly horizontal position is primarily maintained. The elevation of the head-end of the nervous system became necessary for the acquisition of food and for the protection of the animal, and in the present-day series of vertebrates this elevation of the head reaches various degrees. In some vertebrates, particularly in the mammalian class and in birds, the feature is outstanding. As our interest as human beings must essentially be in the phenomenon in man or certainly in the so-called higher orders of mammals, we find the problem of erect posture in its effect upon pressure-conditions about the central nervous system of great importance. While in the four-footed horizontal mammals the elevation of the head above the rest of the nervous system may be the customary posture, the vertical position may be momentarily assumed in climbing, rearing and other movements of the kind. In man, however, and in the erect and semi-erect primates, the habitual vertical posture imposes in extraordinary ways hydrostatic pressure-changes about the central nervous system—hydrostatic pressures which are dependent upon the continuous column of cerebrospinal fluid in the subarachnoid space. For this fluid-space about the whole central nervous system is a continuous fluid-column: even though traversed by numerous trabeculae it has no anatomical structures which could even remotely be considered as potential valves capable of interrupting a fluid-column.

With the existence in erect man of such a hydrostatic fluid-column in the subarachnoid space, it is interesting to note that until the last few decades no attention has been paid by physiologists, and but little by clinicians, to its possible effect on pressure-relationships in the horizontal and erect postures, even though physiologists had made many studies of the alterations in the cardio-vascular system attendant upon change from the horizontal to the erect position. The reason for the almost total lack of detailed study of the effect of positional change upon pressures about the nervous system lies, I believe, in the fact that thought in this field has been so largely dominated by a doctrine of fundamental importance to the whole problem,—a doctrine a century

and a half old, one promulgated by one of the most distinguished of the eighteenth century group of Scotch anatomists, Alexander Monro secundus. Any discussion of the hydrostatics of the cerebrospinal fluid necessarily gives full weight to this hypothesis of constant volume within the bony coverings of the central nervous system.

In 1783 Monro (10) first advanced the thesis that the blood circulating within the cranium must at all times be of constant volume. Monro's reasoning was that "as the substance of the brain, like that of other solids of the body, is nearly incompressible, the quantity of blood within the head must be the same, or very nearly the same." The basis for this hypothesis was Monro's anatomical generalization that the brain is "enclosed in a case of bone" and it therefore followed that within such a rigid-walled container, the contents must at all times be the same. Considering the brain to be of unchanging volume and having no knowledge of the cerebrospinal fluid, Monro was logically led to the assumption of a constant intracranial content of blood.

Monro's concept, developed and apparently verified by Kellie (7) so that it has become known as the Monro-Kellie doctrine, has not descended through these one hundred and fifty years without additions and amendments. Burrows (3), largely on the basis of Magendie's (9) descriptions, introduced the cerebrospinal fluid into the hypothesis; and while his findings did not coincide exactly with those of Kellie, he accepted the basic reasoning of the hypothesis, assuming a constant intracranial volume with the blood and cerebrospinal fluid serving as the two reciprocally variable elements.

While originally restricted to the cranium, the doctrine of a rigid container of the central nervous system with a fixed and constant capacity has necessarily been extended to include the vertebral portion of the system, with the arches affording the necessary rigidity for firm suspension of the spinal dural sac within the epidural space. The type of evidence giving origin to the hypothesis was purely anatomical; then came apparent support from observations of the intracranial blood-volumes in dead animals on vertical suspensions. Subsequently a series of inconclusive experiments with direct inspections of the cerebral blood vessels through cranial windows aroused certain doubts of the accuracy of the doctrine, and finally, twenty to thirty years ago, measurements of intracranial venous pressure and cerebrospinal fluid

pressure caused some investigators to discard the idea of constancy of intracranial volume while others reaffirmed it on the basis of almost identical observations.

My own interest in the Monro-Kellie hypothesis of constant volume within rigid skull and vertebral column became acute some fourteen years ago through an initial study of dehydration of the central nervous system—originally experimental work (19, 20) but now, due largely to the efforts of a group of neurological surgeons here in Philadelphia, widened into clinical procedures of significance. The dehydration of the nervous system was accomplished by the intravenous injection of strongly hypertonic solutions, which markedly reduced the pressure of the cerebrospinal fluid, frequently producing negative values. These findings were immediately related to the Monro-Kellie doctrine of fixed intracranial contents and particularly to that part of the hypothesis pertaining to the rigid character of the container. The conclusion was inevitable that negative pressures (*i.e.*, below atmospheric) could be obtained only if the walls of the container were sufficiently rigid to withstand collapse when fluid was abstracted from the nervous tissues and from the cerebrospinal fluid—sufficiently rigid to prevent the direct application of atmospheric pressure upon the dural sac and its contents.

With this general verification of the function of the total container protecting the nervous system from atmospheric pressure, other studies have led to a determination of some of the limits of accuracy of the thesis. In the literature of the subject, Kellie (7) and Ecker (4) had commented upon the variation in cerebral blood-volume in intact and trephined animals, suggesting thereby a functional significance of the cranium in the process. This importance of the cranium to the protection of the nervous system has been demonstrated (18) by additional experimental procedures employing dehydration; the data yielded indicated that within the physiological limits tested the cranium introduced a factor of rigidity of fundamental importance to the maintenance of the closed character of the container of the central nervous system. But all these experiments based on dehydration dealt with profound and drastic changes in the pressure of the cerebrospinal fluid and were not such as to give information of the potentialities of certain hypothetical elastic factors, such as the vascular readjustments

within the nervous system, the collapsibility and expansibility of the spinal dural envelope, the stretching of the epidural trabeculae, the dilatation of the epidural venous plexus, the elasticity of the occipito-atlantoid ligament, and others of similar kind. These factors seemed to be of utmost significance in determining such alterations in the pressure of the cerebrospinal fluid, as the assumption of a vertical posture might impose upon the nervous system. Were the spinal dural tube so supported within the epidural space that it could not collapse inward, were its fibrous architecture of such small elasticity that outward distensibility were hardly measurable, were the cranium with its adherent dura a rigid box-like container, and were the vascular regulatory mechanisms of the intradural contents so effective that no volume-change nor dislocation of blood would occur—if these suppositions were correct, the measurable pressures of the cerebrospinal fluid in the horizontal position would be reproduced in the vertical position of the mammal, for this assumed rigidity would then be such as to prevent a dislocation of fluid from the uppermost portions of the system to the lowermost. Such potential dislocation of fluid would be necessary for measurable alterations in pressure even though in such positional change the vertical column of molecules theoretically imposed upon the lowermost portion would undoubtedly effect a pressure-change within the fluid itself.

With these potentialities before one, it becomes of interest to analyze the results of experiments (13) involving the abrupt tilting of anesthetized animals from the horizontal to the two vertical positions, with measurement of the pressures of the cerebrospinal fluid and of the cerebral venous sinus. Using dogs of spinal length of 400 mm., it has been found that tilting to the vertical head-down position increases the pressure of the occipital cerebrospinal fluid slightly over 100 mm. of saline solution, while the contrariwise tilting to the vertical tail-down position decreases this pressure by approximately 75 mm. In such dogs of a uniform size and weight, the 400 mm. of vertebral column represent the length of the column of fluid in the subarachnoid space which might theoretically be imposed upon the existing pressures of the horizontal position. Were not elastic elements present within the cranio-vertebral system (and particularly within the intradural

contents), no change in measurable pressures on such positional changes should be recorded; the increase and decrease in pressure of the cerebrospinal fluid on such positional change must therefore be looked upon as being due to a dislocation of fluid from the uppermost to the lowermost portions of the subarachnoid space. The extent of the pressure-changes occurring in the cerebrospinal fluid on such tilting indicates that only one-third to one-fourth of the height of the continuous fluid-column of the spinal subarachnoid space is effective. In other words, there is partial rather than complete protection of the central nervous system against the full effects of hydrostatic pressure. This protection of the central nervous system serves also against the application of atmospheric pressure, as can be demonstrated by combined occipital and lumbar punctures in the horizontal position, with subsequent tilting of the animal to one of the two vertical positions. In such a case, air will rush into the upper needle and a pressure-change of almost double the usual extent will be recorded in the lower manometer. Or by complete laminectomy throughout the lumbar and thoracic regions (15), atmospheric pressure can be directly applied to the exposed spinal dura mater. Under these conditions, tilting the animal to the vertical tail-down position gives the same pressure-change as in the intact preparation, but the head-down vertical tilt results in a pressure increase of 185 mm., as compared to 105 mm. in the normal intact animal.

As a logical outgrowth of these findings came the direct determination of the coefficient of elasticity of the dural sac and its contents (16, 5, 17). This computation was made by measurement of the amount of cerebrospinal fluid dislocated into or from open-end manometers of various calibers on tilting, with simultaneous measurement of the pressure-changes in the cerebrospinal fluid. These calculations gave differences in the volume-changes of the cerebrospinal fluid and differences in the pressure-changes. These differences in pressure-changes (dP) and in volume-changes (dV) were found to have a constant relationship in any one animal, and the fraction dV/dP was ascertained to be of a definite value in the different age-groups in dogs, cats and macaques. The fraction of dV/dP could then be substituted into the general physical formula for the determination of the coefficient of elasticity. This coefficient is defined as the quotient of the stress by

the strain. The stress is the difference in pressure (dP) and the strain the difference in volume (dV) divided by the original volume (V), or $E = dP/\frac{dV}{V}$.

With the determination of the original volume as the contents of the dural sacs, both cranial and spinal, definite values of the coefficient of elasticity were obtained for the various age-groups in the three mammals. The youngest group (immature, juvenile animals) had a larger coefficient of elasticity than the young adult group, which in turn exceeded that of the wholly adult group and in turn the group of old animals.

From the standpoint of the present discussion, it is significant that the values of dV/dP were found to be of the same magnitude on head-down and tail-down vertical tiltings. This identity of values occurred in the original series in four out of every five dogs, and in fourteen out of fifteen cats, and in four out of every five monkeys.

It is probably of importance that a physical formula, used for the determination of the coefficient of elasticity of solids, fluids and gases on compression can be applied with profit to the problems of meningeal elasticity, so that the relationship of external dislocation of cerebrospinal fluid to its resultant pressure may be expressed as a fraction with the constant value for any one animal. In the case of the central nervous system, it is apparent that the phenomena under consideration are not those of ordinary compression of the contents of the intradural cavity nor those of possible dilatation of its contents under conditions of reduced pressure. It seems clear that the changes in volume with pressure are due to the elasticity of the membranes and of the vascular bed which permits not only an internal shift of the fluid from one part of the nervous system to another but also an external dislocation into or from manometers during positional change. It is surprising that the total effect produced by a complex system containing elements with different degrees of elasticity can be expressed by one general coefficient of elasticity which is so nearly constant in animals of the same species, even though differing somewhat in age. Were intact animals to be tilted from the horizontal to the two vertical positions, an internal dislocation of fluid would unquestionably occur but it would occur without any appreciable change in the total volume of the intradural

contents. In the experiments recorded, the total volume of the intradural contents may be taken to vary at the maximum only to the extent of the amount of dislocation of fluid into or from the external system. Under these conditions, any intradural volume-change is at least in part compensated for by reciprocal variation of blood-volume within the dural sac. The importance of such reciprocal elements to this whole problem cannot be over-stated, but the limitations of this essay do not permit me to enter upon detailed discussion of this topic.

All of these data, derived from experiments dealing with the abrupt tilting of mammals from the horizontal to the two vertical positions, really allow a re-casting of the Monro-Kellie doctrine (14). Interpretation of the findings leads to a concept of the central nervous system being enclosed within a rigid container but encompassed by membranes and vascular channels possessing a definite elasticity. The intradural cavity may be taken to be completely filled by central nervous system, by blood and by cerebrospinal fluid; its volume is, under normal conditions in the intact animal, apparently constant. The cranial walls and vertebral arches may be looked upon as affording rigidity to the whole system and as protecting it from atmospheric pressure; but there is within this bony container a complex elastic element, constituted of the spinal dural sac and also of the blood vascular channels within the nervous system and the meninges. This elastic element permits in the intact animal a dislocation of fluid from one part of the nervous system to another without appreciable change in volume. The observations made on cats, dogs and macaques indicate that the coefficient of elasticity of the dural sac and its contents in these three mammals is of approximately the same magnitude; and it seems fair to conclude that somewhat similar values may be found to hold throughout the mammalian class. It is important to realize that the experiments dealing with tilting from the horizontal to the two vertical positions unquestionably fall within the normal limits of the elastic system; the two vertical positions may represent abnormal or seldom employed postures during life but they are within the range of possible performances.

In the light of such re-casting of the Monro-Kellie hypothesis, the application of these experimental findings to the general problem of pressure-conditions about the central nervous system of mammals, which have assumed the semi-erect or erect posture for a considerable

portion of their daily life, yields much in the way of suggestive hypothesis. While these experimental data have been derived from anesthetized mammals, such fragmentary observations as we have from human beings indicate the general application of the findings. A number of clinical observers (Barré and Schrapf (2), Zylberlast-Zand (22), Pfaundler(11), Ayer (1), Howe (6), and others) have reported that cerebrospinal fluid pressure at lumbar puncture is considerably higher when determined in the sitting than in the prone posture; the average increase in pressure is approximately 200 mm. of normal saline solution. Such an increase in man, where the spinal length is in the neighborhood of 600 mm., would fall in line with the pressure-decrease of the vertical tail-down position in the anesthetized dog when measurement is made in the occipital region.

Somewhat similar data from clinical practice have been reported by Ayer (1), who found the pressure in the cisterna magna in man in the erect posture to be below zero; *i.e.*, less than atmospheric. This finding is in accord with Walter's conclusion (12), based on study of clinical cases with cranial defects, that in erect man the level of atmospheric pressure is in the mid-thoracic region; he has estimated that the pressure in the subarachnoid space in the vertex region would be minus 200 to minus 400 mm. of salt solution. With this important deduction of Walter's, the findings in anesthetized mammals unquestionably agree. Giving due consideration to differences in spinal length, the projection of atmospheric levels from the menisci of open-end manometers in the two erect positions always falls within the animal's body, thus indicating that those portions of the subarachnoid space above the level of the projection are under pressures less than atmospheric. In other words, in the two vertical positions the uppermost portion of the animal's central nervous system is under negative pressure, while the lowermost portion is under pressures above the normal level of the horizontal position. Such deductions are in accord with the isolated observation of Krönig and Gauss (8) on a single calf, and with their observations upon cadavers subjected to partial tilting.

These assumptions derived from the experiments on animals, from clinical observations, and from the questionable findings on cadavers, hold for the catarrhine monkey as well as for the four-footed mammals (cat, dog) whose normal postures are horizontal and whose heads are

customarily carried at levels but slightly above those of the horizontal spinal cord. The macaque, while still exhibiting four-footed progression, lives as large a proportion of his life in the erect posture as does man; the pressure-changes in the cerebrospinal fluid of the macaque are of the same relative magnitudes as are those of the cat and dog. The coefficient of elasticity of this monkey's intradural sac and its contents is the same whether derived from head-down or tail-down tiltings. The fractions dV/dP, calculated from pressure-changes and volume-changes in the cerebrospinal fluid on the two types of tilting, are the same. One is inevitably led therefore to the conclusion that evolutionary progression which permitted the assumption of the erect posture by certain of the primates was not accompanied by the development of any special mechanism for the protection of the central nervous system against hydrostatic pressures within the cerebrospinal fluid.

It may be advanced that the experimental data show some additional protection against positional change in the tiltings to the tail-down position (with head-up, erect posture) as the pressure-decreases in the occipital cerebrospinal fluid are less than the increases for the head-down position. This difference is not great (75 mm. as opposed to 105 mm. in intact animals of 400 mm. spinal length) and is to be largely related to the inherent possibilities of inward collapse or expansibility of the spinal dural sac, as well as to certain vasomotor adjustments within the systemic and intracranial venous systems. Such protection as may be afforded by this character of the spinal dural envelope and by the vasomotor readjustments within the venous system is probably of constant magnitude throughout the mammalian class.

Such generalizations involve consideration of the relationship of the pressure of the cerebrospinal fluid to that of the cerebral venous system. This significant relationship cannot be discussed in detail here: suffice it to say that the accepted concept deals with the independence of the pressures of the cerebrospinal fluid and of the cerebral venous system, while acknowledging an influence of the one upon the other. Reliance is placed upon this influence in the clinical use of the Queckenstedt test, where pressure upon the veins of the neck results in an increase in the pressure of the cerebrospinal fluid. The tilting experiments on animals have afforded certain new lines of attack upon the

general problem; but most of the work on this particular aspect of the subject is still in progress and the interpretations of these newer observations are more tentative in nature than are those thus far presented to you. I shall take the liberty therefore of devoting the remaining portion of this hour to a record of findings still unpublished and to some speculation about them, particularly as they relate to the factors concerned in positional changes of intracranial pressures.

In the ultimate analysis, the two elements in the pressure-changes of the cerebrospinal fluid on tilting are (1) hydrostatic pressure and (2) elasticity of the investing structures. Both of these factors affect the two fluids concerned (blood and cerebrospinal fluid) in the resulting pressures on positional change, but the purely hydrostatic effects are modified by the elasticity of the investing structures. Thus the elasticity of the meninges permits, under conditions of such positional alteration, a dislocation of cerebrospinal fluid and allows measurable changes in the pressure of this fluid. Similarly, the hydrostatic pressures of the blood vessels of the body (particularly of the intradural vessels) are not wholly confined within the vascular channels but find reflection in the pressure of the cerebrospinal fluid—a reflection due in turn to the elasticity of the intradural vessel walls. While both of the factors are in fundamental character purely physical in nature, the meningeal elasticity is to be related to the morphological structure of the tissues or meninges themselves. The vessels' elasticity on the other hand is, at least in part, physiological in that control of the vascular lumina may be referred to the vasomotor system. With acceptance of these generalizations, it becomes possible to look upon the pressure-changes in the cerebrospinal fluid as being dependent upon two clearly defined hydrostatic elements. The first of these, which we have termed "the meningeal factor," relates to the hydrostatic changes in the pressure of the cerebrospinal fluid as modified by the elasticity of the meningeal sac and its method of suspension within the body. The second factor, called "the vascular reflection in the cerebrospinal fluid," is the effect of the hydrostatic pressure-change within the intradural blood vessels as this pressure-change becomes modified by the physiological elasticity of the vessels themselves and reflected upon the pressure of the cerebrospinal fluid.

Analysis of the data obtained from many types of tilting experiments

has strongly suggested that the effect of these two factors, meningeal and vascular, are not added the one to the other in such positional changes in the pressure of the cerebrospinal fluid, as has been proposed by many writers, but that the measured pressure-change under conditions of minimal volume-dislocation would seem to be largely determined by the pressure-change in one of the two factors acting in the particular preparation. While it is impossible to give in detail the arguments leading to this view, it will probably aid understanding if I record the type of experimentation affording pertinent data. Animals immediately after death, with blood still fluid within the blood vessels, were used for tilting experiments, as they yielded evidence of the magnitude of the hydrostatic columns operating in the absence of the vasomotor control of the vessels. Such preparations showed almost identical pressure-changes in the occipital cerebrospinal fluid on the two types of vertical tilting; the extent of these pressure-changes was almost twice that in the living animal with intact vasomotor control. Subsequently the effect of the hydrostatic pressure of the blood was excluded by placing animals in a refrigerator until clotting of the blood had occurred, or by subjecting animals to complete vascular injections of gelatine. Such preparations were then tilted and the pressure-changes of the cerebrospinal fluid on both vertical tilts were found to be similar and to approximate 75 mm., as opposed to 105 mm. increase on head-down tiltings and 75 mm. decrease on tail-down tiltings in the intact living animal.

Information from these experimental preparations with solid masses in the vascular channels may be interpreted as showing the purely meningeal factor in the abrupt tilting of animals. The evaluation of the vascular reflection can only be arrived at through somewhat complex reasoning in different types of experiments. But in these analyses, it became apparent, from experiments in which the whole lumbar and thoracic subarachnoid space was isolated by ligation from the upper portion of the nervous system, that the pressure-changes on head-down tiltings were of the same magnitude as before ligation, while due to splanchnic paralysis the tail-down tiltings were of far greater extent. The fact that the exclusion of the spinal subarachnoid space in such preparations had no influence in determining the magnitude of the head-down pressure-increases in the occipital cerebrospinal fluid leads

one to the conclusion that the vascular reflection was capable of maintaining the pressure-change without any contribution from the hydrostatic effects in the spinal column of fluid. In other words, the resultant of these two pressure-effects was determined largely, if not wholly, by the vascular reflection and not by any interaction between the two.

With these data as to the extent of the purely meningeal factor and as to the pressure-change brought about by the vascular reflection alone (as in the dog with ligated spinal cord), it becomes possible to extend the analysis into other experimental animals. On head-down tiltings, the extent of the meningeal factor is unaffected in the living intact animal, in the trephined dog and in the intact animal immediately after death; on the contrariwise tiltings this element is unaffected in the intact animals (living and immediately after death) and in living animals laminectomized throughout lumbar and thoracic regions. In these tail-down tiltings, the pressure-decrease in the living intact animal is of the same magnitude as in the gelatine-injected animal: here again there is determination of the pressure-change almost entirely (if not entirely) by one of the factors—the meningeal.

Consideration of all these data gathered from these tilting experiments leads to the conclusion that in intact living animals the pressure-changes in the cerebrospinal fluid will always be the same as, or will exceed, the pressure-changes of the purely meningeal factor as ascertained in dogs with solid masses in the blood-vessels. A pressure-change in the cerebral veins of considerably greater magnitude than the meningeal factor is necessary to affect this minimal pressure-change in the cerebrospinal fluid—a minimum determined by the meningeal factor. When the pressure-change in the cerebral veins achieves the necessary magnitude to affect the pressure-alteration in the cerebrospinal fluid, this venous pressure-change will continue to be reflected in the cerebrospinal fluid to the same extent, irrespective of change in the meningeal factor. On the other hand, the minimal pressure-change in the cerebrospinal fluid, as determined by the meningeal factor, can be altered by change in the meningeal fluid-column, but only when the vascular reflection is ineffective.

The apparent complexities of these physiological arrangements regarding the two factors concerned in these positional pressure-changes about the central nervous system, become somewhat clearer if one

examine data obtained from attempts to determine the influence of pressure-change in the cerebrospinal fluid upon pressure-change in the cerebral venous channels. In these unreported observations, the experimental procedure consisted of tilting animals from the horizontal to the two vertical positions with simultaneous measurement of the pressure in the superior sagittal sinus and of the pressure of the cerebrospinal fluid, by open-end manometers of various bores. In a series of 18 dogs of average spinal length of 400 mm., 17 of the animals showed no effect in sagittal pressures, of diminishing pressure-change in the cerebrospinal fluid. One animal alone exhibited, in the tilting with an 8 mm. manometer, a slight but definite falling-off in the pressure-change of the superior sagittal sinus.

These findings, indicating a lack of influence of pressure-change in the cerebrospinal fluid upon pressure-change in the sagittal sinus, are in one way essential to the hypothesis that the positional pressure-alterations in the cerebrospinal fluid may be determined by either of the two factors—meningeal element or vascular reflection. Yet in one other wholly important way they would seem to contradict this hypothesis, for the constant pressure-change in the sagittal sinus—here giving rise to the greater of the two factors—should in this interpretation be followed by constant pressure-change in the cerebrospinal fluid, *i.e.*, the larger manometers should all show the same pressure-alteration as the 1 mm. manometer. But here another element makes its appearance in the story. All of the previous pressure-changes reported have been determined with the 1 mm. manometer in which the extent of changes in the pressure of the cerebrospinal fluid are quite similar to those of the bubble manometer (measuring pressure without dislocation of fluid) and in which the quantity of fluid displaced into or from the open-end manometer is so small as to be easily accommodated by the animal. In the experiments with manometers of larger calibers, a greater and greater dislocation of fluid occurred. Such volume-change in the system apparently accounts for the diminishing pressure-changes in the cerebrospinal fluid even when the sagittal pressure-change is maintained fairly constant through vasomotor control.

The reason for the assumption of volume-change as an active factor in the findings with systems permitting an external dislocation of

cerebrospinal fluid is based on similar experiments on dogs immediately after death where the blood is still fluid within the vessels. The same phenomena of decreasing pressure-change in the cerebrospinal fluid on tilting with the larger and larger manometers, and of constant pressure-change in the sagittal sinus, are observed. But in these dead animals, a limit to the volume of displaced fluid is to be noted with the larger manometers; as soon as this limit of volume-displacement is reached, the pressure-changes with the larger manometers are determined by this maximum volume-displacement. While this limit varies on the head-down and tail-down tiltings in some animals, in others it is of the same magnitude on the two tiltings. Such findings and interpretations lead one to introduce into all considerations of the pressure-changes in the cerebrospinl fluid the general question of intracranial volumes—both of the blood and cerebrospinal fluid.

With these more recent data before one, it becomes possible to speculate upon the whys and the wherefores of some of the physiological readjustments about the central nervous system to positional change. From the evidence at hand it must be acknowledged that almost all erect mammals have pressures below atmospheric in cranial subarachnoid space. Such negative pressures must have an important bearing upon all of the physiological needs of the encephalic portion of the central nervous system. It may be a matter of importance that none of the animals whose habitual posture is semi-erect or erect has a spinal length much in excess of that of man, but the elevation of the head in some of the mammalian forms reaches limits unencountered in the erect series of primates. The most extreme example of this phenomenon is found in the giraffe. In a fully grown, adult male of this species the head may be as much as 3 meters (almost 10 feet) above the lumbar spinal region. While information is of course lacking regarding the cerebrospinal fluid pressure in such animals in the horizontal position, it will probably be found to be that of other mammals, about 125 mm. of salt solution. If one apply the general process of reasoning from pressure-changes on tilting in other mammals, the level of atmospheric pressure in the standing giraffe would be about at the base of his neck, while at his vertex there would exist a negative pressure of approximately 2200 mm. of salt solution (minus 160 mm. of mercury). Has this negative pressure in the cranium any

possible purpose, or is it just a chance happening which evolutionary progression has failed to meet by specific adjustment? In the case of the giraffe, where data are lacking and where speculation must inevitably be followed, one wonders about the blood supply to the relatively small cerebral hemispheres. The vertical distance of 3 meters, which this mammal's brain may have above the heart, means that arterial blood must be projected to this extraordinary height through the carotid system. If the pressure in the aortic arch is in the neighborhood of 150 mm. of mercury, as in other mammals, this arterial pressure would not quite be sufficient to overcome the hydrostatic height of the continuous column of carotid blood. With this problem before one, one cannot fail to recall the earliest measurements of arterial pressure by the Rev. Stephen Hales in 1733. Connecting the femoral artery of a horse to a vertical glass tube, Dr. Hales observed the arterial blood to mount to a height of 8 feet 3 inches. Such arterial pressures, if they exist in the giraffe, would hardly suffice to force the blood into the cranium; one fancies therefore that possibly an explanation lies in the hydrostatic effects in the cerebrospinal fluid. The existence of a negative pressure within the cranium would unquestionably facilitate the maintenance of a cerebral arterial supply, and it may be that the negative pressures within the crania of all erect mammals have at least some rôle in securing adequate blood supplies for the hemispheres. From the venous standpoint, with the possibility of negative pressures occurring within the subarachnoid space on positional change, it would seem essential that a mechanism be had which would preserve a fairly constant venous pressure-alteration. Such a mechanism seems to be indicated by the constancy of the sagittal pressure-changes on tilting animals with different-sized manometers, where the pressure-changes and the volume-changes in the cerebrospinal fluid were of different magnitudes. Perhaps here again one may reason teleologically.

But such suggestions and fantasies lead one far from the field of absolute knowledge. Is not this whole question of intracranial pressure-changes opening up for additional steps which will advance our knowledge of the subject? There seems to be every reason to accept the general thesis of negative pressures within the crania of erect mammals. Yet acceptance of this thesis leads one into many inquir-

ies, some of immediate clinical importance, such as the occurrence of cerebrospinal rhinorrhea, for cerebrospinal fluid could drip from the nose only with a positive pressure within the cerebral ventricles and cranial subarachnoid space. Does this fluid escape only in the prone position or do all of these cases have air within the closed cranial box? Will not our ideas of the methods of the production and absorption of the cerebrospinal fluid, drawn today largely from experiments on four-footed animals, now have to be re-investigated from the standpoint of positional shifts in the pressure of the cerebrospinal fluid and in intracranial venous pressure? Shall we not have to differentiate clearly between the effect of cerebral venous pressure-change and cerebral venous volume-change? Are not all of these questions intimately connected with the problems of the neurological surgeon who is confronted with the expert handling of a fluid-system within a rigid-walled container which after all embraces confusing elements of elasticity? Will not postural changes be shown in subtemporal decompressions, and will not the absence of collapse in the cranial defect in such patients indicate an abnormality within the central nervous system or its fluid-bed? Does not the introduction of a known element of elasticity into the Monro-Kellie doctrine afford a more adequate base for proper neurosurgical procedures, for is not the surgeon now given definite information as to the extent of the hydrostatic shifts in the pressure of the cerebrospinal fluid?

Yet these are but a few of the questions which advance in factual data pertaining to positional alterations in the pressures about the central nervous system has presented to our consideration. In some ways, however, we have not progressed far beyond the original conception of Alexander Monro. We are able to introduce a definite element of elasticity into the concept—at least for the dog, the cat, and the macaque. Information regarding this element of elasticity in man should be forthcoming soon and our hypothesis will then rest upon a firmer basis. But meanwhile, is it not safe to conclude that the central nervous system is largely protected from the full effects of atmospheric pressure by the bony cranium and bony vertebral canal; and that within such a bony encasement we have a fluid-containing sac of fairly constant volume? This constancy of volume is apparently maintained, but dislocations of fluid from one part of the system to another, per-

mitted by the elasticity of the system, result in important pressure-changes. With this idea of a constant volume of the container of the central nervous system, the Monro-Kellie hypothesis in its original statement is in accord. Recent studies have added much to our knowledge of positional alterations—but we are on safest ground when we pattern our concepts of pressure-conditions about the central nervous system against the background of the Monro-Kellie hypothesis.

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BILIRUBIN EXCRETION AS A TEST FOR LIVER FUNCTION DURING NORMAL PREGNANCY

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The functional integrity of the liver during pregnancy has always been a subject of great interest and considerable confusion to the obstetrician. The fact that during certain pathological states of pregnancy, notably "Hyperemesis Gravidarum" and the so-called hepatic type of eclampsia, definite histological alterations are demonstrable in this organ has led many investigators to believe that changes may occur in the liver during normal gestation that render it peculiarly susceptible to the more severe affections, such as those toxemias which occur in the latter half of pregnancy. It is conceivable that as a result of the increased maternal demands during the normal gestation, the physiologic processes of the liver are subjected to extra stress which may be discernible either microscopically or through an investigation of its functions.

Hofbauer (1) in 1907 described what he thought were typical changes occurring in the liver of normal pregnant women. He spoke of this as the "Schwangerschaft's Leber." These changes were characterized by fat infiltrations in the cells in the central part of the lobule, dilatation of the bile channels, central vein and afferent capillaries. These findings, however, could not be confirmed by several later investigators notably Schickele (2) and Heinreichsdorf (3). Opitz (4), on the other hand, found that there is frequently an abnormal deposit of fat in the liver in pregnancy. Schickele (2) has also shown that fatty infiltration occurs in the liver of pregnant animals.

Simultaneously with the attempts to demonstrate pathological changes in the liver various means were employed to determine the state of its function during normal gestation. Walthard (5, 6) found that in uncomplicated pregnancy there tends to be a hyperglycemia

and an impairment of the ability of the liver to store glycogen as well as an increase in the urobilin content of the urine. Heyn and Messtorf (7), as well as Couinaud and Clogne (8), observed the Widal hemoclastic test to be positive in about one-third of a series of healthy women in the late months of pregnancy. Seitz (9) conducted a series of studies on the liver function of twenty-five normal pregnant women. He found that in over 80 per cent the excretion of uric acid, ammonia and amino acids in the urine was increased. There was an increase in the blood bilirubin in 8 per cent of the cases, while urobilin was increased in the urine in 64 per cent of the instances studied. He also observed a change in the carbohydrate metabolism, since a longer period of time was required by the pregnant patient to assimilate a given amount of levulose as compared with the normal non-pregnant woman. He also expressed doubt, however, as to whether these changes could be attributed to an altered function of the liver. Siegel (10) studied the liver function of sixty normal pregnant women by means of the bromsulphthalein test and found normal elimination of the injected dye at the end of one-half hour in all instances. Cross (11) conducted an elaborate study on sixty-one normal pregnant women, employing seven different tests to determine liver function. These were the bromsulphathalein test, the levulose tolerance test, the hemoclastic crisis of Widal, the Van den Bergh reaction, the Fouchet test, the icterus index and, finally, the Ehrlich and Schlesinger tests for urobilinogen and urobilin in the urine. He found that in all the normal subjects the various tests employed yielded uniformly negative results. Herold (12) studied the changes in the amount of urinary pigment in pregnancy by means of a modified photomotor and found that no increase occurs during normal gestation. He interpreted this as evidence of normal liver function.

The brief review of the literature just presented demonstrates the variety of opinions that exist concerning the function of the liver during the normal pregnant state. The small amount of positive evidence may very well be criticized on the grounds that it does not necessarily reflect the function of the liver. The more specific tests have yielded uniformly negative findings. This may be construed to be due to the fact that the liver does not undergo any alterations in its function during normal gestation but, on the other hand, it may be

due to inadequacies on the part of the tests employed to detect slight changes in function.

In 1927 von Bergmann (13) and his associate Eilbott (14) studied various hepatic disorders by noting the rate of excretion of intravenously injected bilirubin. Harrop and Barron (15), working in this clinic, conducted similar studies with this method and obtained satisfactory results. They conclude that "the bilirubin excretory power of the liver is the most delicate method so far proposed for testing the functional capacity of this organ." My own experience with this test has led me to subscribe to their opinion. The method is capable of

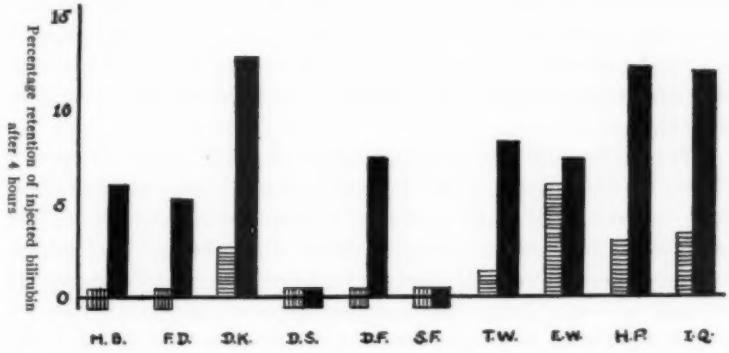

FIG. 1. DEGREE OF RETENTION OF INJECTED BILIRUBIN DURING THE FIRST AND SECOND HALVES OF PREGNANCY

First half of pregnancy. Second half of pregnancy.

demonstrating evidence of impaired function in instances in which the liver injury is slight and in which the tests that are usually employed yield no evidence of hepatic disturbances.

Employing the bilirubin test as well as the levulose tolerance test and the initial hyperglycemic reaction after insulin injection, Kaufmann (16, 17) studied the liver function of twenty-six normal pregnant women. He found that in the latter half of pregnancy all but three of his patients showed impaired function as demonstrated by either one or the other of the tests employed. Sixteen of these patients were investigated with the bilirubin test and, of these, eight showed an

abnormal response. The results with the other two tests were essentially the same. Certain objections arise, however, in reference to Kaufmann's work. Those patients who were studied in the later months of pregnancy were not investigated during the first half. His conclusions would be much more convincing if an actual change in the excretion of the injected bilirubin or in the assimilation of carbohydrates could be demonstrated as the patient progressed from the early to the later stage of pregnancy. The fact that only 50 per cent of Kaufmann's cases show impaired liver function, by means of the bilirubin test alone, may be due to the employment of a uniform dosage of the material, 50 milligrams, for all patients. In our studies we have found it advisable to regulate the amount of bilirubin used according to the weight of the individual patient. The degree of retention after the end of 4 hours which he considered to be within the normal range, 15 per cent, according to my experience is too high a value.

The present study was made upon patients in the obstetrical service of this hospital. Twenty-one normal pregnant women were studied, upon whom a total of 31 tests with bilirubin were performed. Ten of these 21 patients were studied during both the first and second halves of pregnancy. The patients were followed carefully in the obstetrical out-patient department of the Johns Hopkins Hospital and during the period of observation no abnormalities were noted in the course of their pregnancies. All the patients were delivered of normal babies at term.[1]

METHOD

We have received numerous inquiries during the past three years on the technique of the bilirubin test employed in this clinic. The details therefore are given below together with certain improvements which I have developed during this period.

The bilirubin employed was obtained from the Eastman Kodak

[1] I wish to express my indebtedness to Dr. Arthur Koff of the Department of Obstetrics for the selection and observation of the cases studied, and to Dr. H. J. Stander, Acting Head of the Department of Obstetrics, who purchased for me part of the bilirubin used in this investigation.

Company and the Chemisch-Pharmaceutische A.G., Bad Homburg, Germany. The test is performed as follows: One milligram of bilirubin per kilogram of body-weight is dissolved in 15 cubic centimeters of 0.1 molar solution of sodium carbonate, which has been previously brought to the boiling point and then allowed to cool to 80°C. I have found that a 0.1 molar solution of the sodium carbonate is a much better solvent of bilirubin than the 0.5 molar solution originally employed by Harrop and Barron (15). The further advantage of the more dilute solution of sodium carbonate lies in the fact that accidental extravasation into the surrounding tissue is associated with much less pain and injury to the tissue than would occur with a 0.5 molar solution. The bilirubin dissolves completely and a clear iodine-colored solution is obtained. A control sample of oxalated blood is collected in a perfectly dry syringe to prevent hemolysis and the dissolved bilirubin is then injected intravenously. Oxalated samples of blood are obtained from the other arm in five minutes, when complete mixing has taken place, and again four hours after the injection. No untoward reactions, such as fever, flushing or chills were observed in any of the patients studied. The amount of bilirubin in the plasma is determined by means of the Ernst and Förster method (18). The plasma is precipitated by redistilled acetone, which is used at different concentrations, depending on the amount of bilirubin in the sample. Thus, in the control and in the four-hour samples, to 2 cubic centimeters of plasma there are added 2 cubic centimeters of acetone, while with 1 cubic centimeter of the plasma of the five-minute specimen 4 cubic centimeters of acetone are used. After shaking the plasma and acetone mixtures, the samples are centrifuged and filtered directly into a colorimeter cup and compared with a standard composed of 1 to 6000 potassium bichromate solution, which has been previously standardized against a known solution of bilirubin. All the glassware used, including the colorimeter cups, must be perfectly dry and clean. The acetone solutions of bilirubin must be protected from the light except during the actual reading in the colorimeter. The bilirubin content of the specimen taken five minutes after the injection minus that of the control sample is considered as containing 100 per cent of the injected pigment. The percentage of bilirubin retained in the four-hour sample is then calculated after previous subtraction of the

bilirubin contained in the control. The following formulae are employed to determine the amount of bilirubin in the various samples:

$$\text{Control and 4-hour specimens} - {}^{*}0.329 \times 2 \text{ (dilution)} \times \frac{\text{Reading of Standard}}{\text{Reading of Unknown}}$$

$$\text{5-minute specimen} - {}^{*}0.329 \times 5 \text{ (dilution)} \times \frac{\text{Reading of Standard}}{\text{Reading of Unknown}}$$

* 0.329 mg. per cent of blood bilirubin corresponds in color to a 1 to 6000 solution of potassium dichromate.

In most instances all of the bilirubin disappears from the blood stream after 4 hours. Rarely, as much as 5 per cent of the pigment is still retained in normal individuals after this period of time. Retention beyond this point was considered pathological. Since a certain amount of familiarity with the procedure is required to compare accurately the colors of the known and unknown solutions, it is advisable to have one individual make all the readings at one time. This was the procedure followed in this investigation.

RESULTS

Table I records all of the patients studied. Eleven were investigated from the 2nd to 4th month of pregnancy while 10 were studied from the 5th to the 9th month. Of the 11 instances, in the first half only one (E. W.) showed a retention after 4 hours which was considered abnormal. In the second half of pregnancy all of the patients except one (L. F.) showed distinctly abnormal degrees of retention of the injected pigment, the extent of retention varying from 5 to 23 per cent. The average amount of bilirubin in the blood stream after 4 hours in those patients studied during the first 4 months of pregnancy was 1.5 per cent, while from the 5th to the 9th month the average was 10.5 per cent.

Although data of this type are suggestive, much more convincing evidence is obtained if one group of patients is followed throughout pregnancy. Table II represents such a series. Ten normal pregnant women were studied during the first and second halves of pregnancy. Of this group there were two patients (D. S. and S. L.) who failed to show any alteration in liver function with progression of gestation, while one patient (E. W.) showed an abnormal retention of injected

bilirubin during the early and late stage of pregnancy with a slight increase in the degree of retention in the second half. In none of these women was the degree of retention during the first 4 months greater then during the last 5 months.

TABLE I

*Degree of retention of injected bilirubin during various months of pregnancy**

NAME	PERIOD OF GESTATION	EARLY VOMITING OF PREGNANCY	GRAVIDA	BILIRUBIN RETENTION
	months			*per cent*
D. P.	3½	no	4	0
M. B.	3½	yes	2	0
E. D.	2½	yes	2	0
D. K.	2½	no	5	2.7
D. S.	3½	yes	1	0
D. F.	4	yes	8	0
S. F.	2½	yes	7	0
T. W.	3½	no	1	1.3
H. P.	4	no	1	2.9
I. Q.	4	no	3	3.4
E. W.	2	yes	1	6
Average				1.5
M. R.	5	yes	3	11.1
M. Ro.	5	yes	4	23.1
Mrs. Y.	5			11.5
E. B.	6½	no	5	5.4
P. W.	7		3	9.0
M. Br.	7	yes	6	15.1
L. G.	8½	yes	4	13.6
M. W.	8		2	7.3
M. Bra.	8½	no	5	7.6
L. F.	9	yes	2	2
Average				10.5

* The Van den Bergh reaction of all the patients listed in this table was negative.

In attempting to seek an explanation of these abnormal changes in the liver function, one's attention is immediately focussed on the relationship of vomiting in the early part of pregnancy to the impairment of function in the latter half. In table III are listed the degrees of pigment retention both in those patients who did not manifest the

TABLE II

*Comparison of retention of injected bilirubin during the 1st and 2nd halves of pregnancy**

NAME	GRAVIDA	EARLY VOMITING OF PREGNANCY	PERIOD OF GESTATION, FIRST HALF	BILIRUBIN RETENTION	PERIOD OF GESTATION, SECOND HALF	BILIRUBIN RETENTION
			months	*per cent*	*months*	*per cent*
M. B.	2	yes	3½	0	7	6
E. D.	2	yes	2½	0	7	5.2
D. K.	5	no	2½	2.7	8	12.9
D. S.	1	yes	4	0	8½	0
D. F.	8	yes	4	0	7	7.2
S. F.	7	yes	2½	0	7	0
T. W.	1	no	3½	1.3	8½	8.2
E. W.	1	yes	2	6.0	7½	7.3
H. P.	1	no	4	2.9	8	12.1
I. Q.	3	no	4	3.4	7½	12.0
Average				1.6		7.1

* The Van den Bergh reaction of all the patients listed in this table was negative.

TABLE III

*Relationship of vomiting to bilirubin retention (second half of pregnancy)**

NAME	VOMITING	BILLIRUBIN RETENTION
		per cent
E. B.	no	5.4
M. Bra.	no	7.6
T. W.	no	8.2
H. P.	no	12.1
D. K.	no	12.9
I. Q.	no	12.0
Average		9.7
M. B.	yes	6.0
E. D.	yes	5.2
D. S.	yes	0.0
D. F.	yes	7.2
S. F.	yes	0.0
E. W.	yes	7.3
M. R.	yes	11.1
M. Br.	yes	15.1
L. G.	yes	13.6
L. F.	yes	2.0
M. Ro.	yes	23.1
Average		8.2

* The Van den Bergh reaction of all the patients listed in this table was negative.

symptom of vomiting and in those who did. No attempt was made to subdivide the latter group into those exhibiting mild and severe grades of vomiting, since it would have been necessary to rely on the patient's impressions and no reliable objective data were possible on this point. The average retention of both groups approximate each other so well that it seems probable that early vomiting exercises no effect on the changes in liver function in the late months of pregnancy.

DISCUSSION

In attempting to interpret the significance of a test applicable to the liver, one should bear in mind the complexity of the various functions of the organ, only a few of which are well understood. Thus the fact that any single test yields negative results need not necessarily mean that there is no hepatic disturbance. The status of the liver can only be satisfactorily ascertained when all of its duties are investigated. An abnormal response to a particular test, however, is significant evidence of impaired liver function.

By means of the bilirubin test, changes in hepatic function are demonstrable in the last half of pregnancy of most women. That these changes are not of a permanent character is shown by the fact that women who had gone through a number of pregnancies previous to the present investigation failed to show any retention of the injected bilirubin during the first four months.

What relationship these changes bear to the subsequent onset of the various toxemias is being investigated at present.

SUMMARY

1. The liver function of 21 normal pregnant women during the various phases of gestation was investigated by means of the bilirubin test. A total of 31 tests were performed.

2. Eleven of the patients were studied during the first four months of pregnancy of which only one showed an abnormal response to the injected pigment. Of the 10 patients studied during the last 5 months all with the exception of one yielded abnormal results.

3. Ten patients were investigated during both the first and the second half of pregnancy. Of these only two failed to show an increase of the injected bilirubin after 4 hours, while one patient, during

the first half of pregnancy, showed an abnormal retention which was increased slightly in the second half.

4. There seems to be no relationship between the vomiting which occurs in the early part of pregnancy and the disturbed liver function in the later period.

5. That the impairment is not a permanent feature is evidenced by the fact that those women who have gone through multiple pregnancies before the present study failed to show any increase in the retention of injected bilirubin during the first four months of gestation.

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BOOK REVIEWS

An Experimental and Clinical Study of Pain in the Pleura, Pericardium and Peritoneum. By JOSEPH A. CAPPS, M.D. and H. COLEMAN, M.D. 1932. Illust. 99 Pp. $3.00. (*The Macmillan Co., New York.*)

This monograph gives the gist of twenty years of experimentation and clinical observation. It is a significant contribution, as emphasizing the importance of localized and referred pain in the diagnosis of diseases of the chest and abdomen. The style is concise and the text adequately illustrated. It is recommended to all students and practitioners of medicine.

E. A. P.

Kolloidreaktionen der Rückenmarkflüssigkeit [Technik, Klinik und Theorie], von DR. MED. WILLY SCHMITT. 1932. 184 Pp. Rmk. 12.50. (*Verlag von Theodor Steinkopff, Dresden und Leipzig.*)

This book handles every aspect of seven of the commoner and better known colloidal reactions, in a detailed, explicit manner. There is a brief consideration of underlying theory and of the relation of these reactions to other spinal fluid constituents. An extensive bibliography is included. A valuable and useful book for anyone working with spinal fluids.

W. W. E., *Sheppard and Enoch Pratt Hospital*

The Cardiac Output of Man in Health and Disease. By ARTHUR GROLLMAN, Ph.D., M.D. 1932. 325 Pp. $4.00. (*Charles C. Thomas, Springfield, Ill. and Baltimore, Md.*)

This, the first monograph on cardiac output, fills a need, sets a standard, and discloses an horizon. It is probably safe to say that future workers and writers in the field will not have to weigh figures earlier than 1932, so critically has the author culled the literature up to the present. This is really the great contribution of the book to the subject, and its main justification. The horizon discovered is that of cardiac output itself, of which present knowledge is meagre, but stimulating.

On page 231, table 48, the average systolic pressure of cases with secondary contracted kidney should be 181 instead of 118.

W. J. T.

Italian Medicine. By ARTURO CASTIGLIONI, M.D. Translated by E. B. Krumbhaar, M.D. [Clio Medica Series]. Illust. 1932. 134 Pp. $1.50. (*Paul B. Hoeber, Inc., New York.*)

Professor Castiglioni's book continues the general excellence of the Clio Medica Series. The illustrations are particularly interesting, some of them having been taken from relatively inaccessible sources. After reading this succinct account,

one cannot but feel that Italy's contribution to medical science is tremendous. The illustrious physicians are briefly discussed. Jeronimo Cardano, however, is not even mentioned, perhaps because he is more often thought of as a mathematician or astrologer than as a medical man.

W. C.

The Anatomy of the Human Orbit and Accessory Organs of Vision. By S. ERNEST WHITNALL. 2nd Edition. 1932. 467 Pp. Illustrations. $6.25. (*Oxford University Press, New York.*)

The second edition of this authoritative book is notable for remarkable additions on the neurology of the eye. The author maintains that the oculomotor nerve contains sensory as well as motor fibers and discusses the proof of the proprioceptive nerve supply of the extrinsic ocular muscles. There are also additional data on paralysis of the abducens nerve and on Gradenigo's Syndrome. The sections on the trigeminal nerve, the nervous control of the iris musculature, the lower visual centers and the nuclear origins of orbital nerves, have been completely rewritten and brought up to date.

There are several additional illustrations of value.

B. R.

Principles of Chemistry. An Introductory Textbook of Inorganic, Organic and Physiological Chemistry for Nurses and Students of Home Economics and Applied Chemistry. With Laboratory Experiments. 1932. Third Edition. 486 Pp. $2.50. (*C. V. Mosby Co., St. Louis, Mo.*)

The additions deal with the elementary principles of physical chemistry and there is a new chapter on foods.

A well-chosen list of questions for study follows each chapter and there is a set of supplementary laboratory experiments at the end.

J. F. S., JR.

Functional Disorders of the Gastro-Intestinal Tract. By WILLIAM GERRY MORGAN, M.D., F.A.C.P. 1932. Illust. 259 Pp. [Everyday Practice Series. Edited by Harlow Brooks]. $5.00. (*J. P. Lippincott Co., Phila., Pa.*)

This is, in all probability, the first book on the subject in English. Being intended for the busy practitioner, it offers no bibliographic or critical review of the literature and no reference to experimentation.

The first part deals with the correlation of the nervous system and the function of digestion. The second covers the motor secretory and sensory neuroses of the stomach, but is reticent on digestive dysfunction and the effects upon the other digestive organs. Gastro-intestinal dysfunction should, of course, be treated as a whole, not as of an organ, or as one phase of an organ's functions. Dr. Morgan recognizes this, in a manner, when he discusses the motor-secretory-sensory affections of the intestines as one. The last part of the volume deals with constipation, flatulence, borborygmus and visceroptosis. The book is clearly and simply written and contains an abundance of case reports with some detailed account as

to therapeutic management. Incidentally, ulcerative colitis, an organic disease, is included.

M. P.

Nutrition and Diet Therapy. A Textbook of Dietetics. By FAIRFAX T. PROUDFIT. 1930. 5th Edition. 705 Pp. $2.75. (*The Macmillan Co., New York.*)

A detailed exposition of dietetics in relation to health and disease, containing removable charts summarizing the biochemical properties of essential food elements and their fate in the body; and the factors influencing food requirements. An instructor's plan for teaching Nutrition, Cookery, and Diet Therapy is included. An excellent textbook for concise reference.

B. B.

Clinical Endocrinology of the Female. By CHARLES MAZER, M.D., F.A.C.S. and LEOPOLD GOLDSTEIN, M.D. 1932. Illust. 492 Pp. (*W. B. Saunders Co., Phila., Pa.*)

This book may be recommended as the best now available on the subject. The presentation is thorough without being too technical for the average reader, while the subdivision of chapters into short sections and the excellent typography make the volume easily approachable. The handling of endocrinology and physiology is not only sound, but reveals excellent discrimination in the separation of wheat from chaff. The chapters on therapy are less satisfying, by reason of the confused and inadequate state of existing knowledge. The authors stress the diagnostic and therapeutic importance of blood and urine hormone studies, perhaps more than is yet justified by accomplished fact. One of the best chapters is the one that describes the various hormone tests for pregnancy, while a valuable asset is the excellent and well selected bibliography, comprising no less than 649 titles.

E. N.

Medicine Among the American Indians. By ERIC STONE, M.D. [Clio Medical Series]. 17 illust. 139 Pp. $1.50. (*Paul B. Hoeber, Inc. New York, 1932.*)

An informing and entertaining book on a subject about which there is much more general misconception than knowledge, from the pen of one man who, starting with a strong antipathy, came to know and admire the folk of whose medical practice he writes. Probably not one practitioner in a thousand has even the vaguest notion of the medicine of the Amerind who once possessed this continent, introduced us to corn and tobacco and added over 50 valuable drugs to the white man's pharmacopoeia. We read of his anticipation of Credé's manoeuvre by centuries, and of a skill in dealing with fractures and dislocations which was passed on to a family of Connecticut bonesetters.

It were well if those who think of the Amerind as a lazy, dirty, comic paper Indian, riddled with tuberculosis and other ills we whites brought him from overseas, could read this account of the rudimentary, but very real skill in medicine possessed by the pre-Colombian inhabitants of this continent.

P. G. S.